

REMARKS

Courtesies extended to Applicants' representatives during the telephone interview(s) conducted on March 15, 2007, during which the rejections asserted in the January 19, 2007, Office Action were discussed, are acknowledged with appreciation. The contents of the interview are reflected herein.

By the present communication, claims 15, 120, 124, 129 and 134 have been amended, and claim 142 has been added. No new matter is introduced as the claimed subject matter is fully supported by the specification and claims as originally filed. In addition, claim 19 has been canceled without prejudice. Entry of the claim amendments submitted herewith is submitted to be proper as the amendments place the present claims in condition for allowance, or at a minimum, in better condition for appeal. Moreover, no more claims are presented for prosecution at this time than have previously been presented for prosecution. Accordingly, entry of the amendments submitted herewith is respectfully requested.

Amendments submitted herewith are not to be construed as a dedication of the subject matter not presently claimed to the public. Applicants reserve the right to pursue claims as originally filed in a continuation application.

With the cancellation of claim 19 and the addition of claim 142 herewith, claims 15-18 and 120-142 are now pending and under active prosecution. A detailed listing of all claims is present in the **Listing of Claims**, beginning on page 2 of this communication, with an appropriate status identifier for each claim. Claims 15-18 and 120-141 are examined and rejected on grounds discussed below. The claim rejections are addressed in the appropriate sections below.

Claims 15, 120, 124, 129 and 134 are amended to define the invention with greater particularity as follows:

In claim 15, line 2 is amended to indicate that the steps of the method are performed in the order presented. Support for this amendment can be found, for example, in the specification in paragraph [0233]. Lines 3-4 are added to include conducting enzymatic assays with molecular scaffold compounds in order to identify those compounds with low to extremely low affinity (per amendment of lines 5-6). Support for enzymatic assays can be found, for example, in the specification in paragraphs [0234]-[0261], and support for scaffold binding with low to extremely low affinity can be found, for example, in the specification in paragraph [0234]. Lines 7-8 are amended to indicate that a derivative is synthesized from the identified molecular scaffold. Support for this amendment is found, for example, in specification paragraph [0025]. Line 9 is amended to indicate that testing of the derivative is by enzymatic assay, as supported, for example, in the specification in paragraphs [0234]-[0261].

Claims 120 and 124 are similarly amended to indicate conducting enzymatic assays to identify molecular scaffolds that bind with low to extremely low affinity, and the synthesis of derivatives of such scaffolds. These claims are further amended to indicate that the derivatives are tested for activity, e.g. by conducting enzymatic assays, to determine whether the derivative has greater specificity or affinity to PIM-1 than the scaffold molecule. Support for these amendments is found, for example, in the specification in paragraphs [0025] and [0234]-[0261].

Claim 129 is amended to indicate conducting enzymatic assays to identify molecular scaffolds, as supported, for example, in the specification in paragraphs [0234]-[0261]. Also, line 4 is amended to indicate that the molecular scaffolds bind with low to extremely low affinity, as supported, for example, in the specification in paragraph [0234]. Line 6 is amended to indicate that chemical structures in the molecular scaffold are identified based on the step of determining the orientation of the scaffold in co-crystals with PIM-1, as supported, for example, in the specification in paragraph [0025].

Claim 134 is amended to indicate conducting enzymatic assays to determine the PIM-1 affinity of a compound of Formulae I, II, or III, as supported, for example, in the specification in

paragraph [0234]-[0261]. The claim is also amended in line 5 to indicate that the compounds bind with low to extremely low affinity, as supported, for example, in the specification in paragraph [0234]. Line 8 is amended to indicate that a ligand is synthesized based on identifying a chemical structure on the compound, as supported, for example, in the specification in paragraph [0025].

Applicants request entry of the foregoing amendments. In view of the preceding amendments and the remarks made herein, the present application is believed to be in condition for allowance.

Previously asserted Rejection under 35 U.S.C. § 102(e)

In the Office Action dated May 31, 2006, claims 15-18 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by US 2004/0146942 ('942). As this rejection was not maintained in the present Office Action, Applicants assume it has been withdrawn and thank the Examiner for this withdrawal.

Rejection under 35 U.S.C. § 103(a) over '942 of Mochizuki in view of U.S. patent 6,197,495, U.S. patent 6,465,484, and WO 01/87887.

Claims 15-19 and 120-141 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over '942 in view of U.S. patent 6,197,495 ('495), U.S. patent 6,465,484 ('484), and WO 01/87887 ('887) or Mochizuki et al. in view of U.S. patent 6,197,495 ('495), U.S. patent 6,465,484 ('484), and WO 01/87887 ('887). Applicants' arguments filed November 2, 2006 were considered, but found unpersuasive. While Applicants maintain traversal of this rejection, in order to reduce the issues and expedite prosecution, this rejection has been rendered moot by the amendments submitted herewith.

Applicants disagree with the Office Action in its characterization of the invention as allegedly requiring three steps carried out *in silico*. For example, the Office Action alleges that the first step involves identifying a scaffold molecule, presumably, using a computer and

available software or by selecting known compounds. As currently amended, claims 15, 120, 124, 129 and 134 indicate that scaffold molecules and the like are not identified by *in silico* methods as they require conducting an enzymatic assay using PIM and molecular scaffold candidates.

The Office Action further alleges that the second and third steps require using said computers and software to identify how the selected compounds bind and to identify derivatives that improve the binding. Still further, it is alleged that the three steps are carried out *in silico*. Applicants point out that in the Restriction Requirement of February 9, 2006, the invention was restricted to, among others, Group I to an *in silico* method of identifying ligands and Group II to an *in vitro* method of identifying ligands. Applicants elected to pursue the Group II claims, directed to *in vitro* methods. Thus, the assertion in the present Office Action that the three steps are carried out *in silico* contradicts the election made in response to this restriction. While the claimed method may involve the use of computers to identify structures to modify within an identified scaffold molecule, some steps in the method are carried out *in vitro*. Claims 15, 120, 124, 129, and 134, as presently amended, use enzymatic assay screening (*in vitro*) to identify compounds with low to extremely low binding affinity (e.g. having a binding constant or IC₅₀ of $\geq 1 \mu\text{M}$), which are then evaluated (*in silico*) to identify ways to modify these compounds. New compounds are then synthesized (*in vitro*) and tested (*in vitro*) for activity. There is nothing in the '942 or Mochizuki references, in view of the '495, '484, and '887 references, that teaches or suggests Applicants' method. The '942 reference provides no suggestion that compounds with low to extremely low affinity would be selected for developing ligands to PIM, nor is this suggested in any of the other references.

In view of the above amendments and remarks, reconsideration and favorable action are respectfully requested. In the event that any matters remain to be resolved in view of this communication, the Examiner is encouraged to call the undersigned so that a prompt disposition of this application can be achieved.

No additional fee is believed due with the present submission. However, the Commissioner is hereby authorized to charge any additional fees which may be required regarding this application, or credit any overpayment, to Deposit Account No. 50-0872. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extensions under 37 C.F.R. § 1.136 and authorizes payment of any such extensions fees to Deposit Account No. 50-0872.

Respectfully submitted,

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